The t(9;11) confers good prognosis in AML patients treated with stem cell transplantation as compared to non-t(9;11) and other adverse-risk abnormalities

To the Editor: In contrast to most translocations affecting the MLL gene, the t(9;11) is not associated with a markedly poor prognosis. Several studies revealed a very favorable outcome in the pediatric patient group. In adult AML, the t(9;11) has also been associated with superior survival, at least compared to other 11q23 abnormalities. Therefore, 11q23 rearrangements in adult AML are now often dichotomized into t(9;11) and non-t(9;11), with the former being included in the intermediate-risk group and the latter in the adverse-risk group. The proposed European Leukemia Net (ELN) cytogenetic reporting criteria reflect this division. We investigated whether the outcome of AML patients treated with allogeneic hematopoietic stem cell transplantation (HSCT) with t(9;11) remains significantly different from the rest of the adverse-risk cytogenetic group.

Conventional cytogenetics and FISH data from diagnostic bone marrow of 110 adult AML patients treated with HSCT (**Table 1**) was reviewed and patients were classified according to the recommendations of the European Leukemia Net and included 32 with favorable risk, 60 in the intermediate-risk group, and 18 in the adverse-risk group. FISH confirmed MLL rearrangement in cases with apparent 11q23 abnormalities. We compared outcome of patients with t(9;11) to the group of patients with adverse-risk cytogenetics that included all MLL-positive non-t(9;11), among other cytogenetic abnormalities classified adverse-risk. Our study included 62 (56%) patients treated in first remission (CR1), while most non-CR1 AML patients were treated with HSCT in CR2. Patients were between 14 and 57 years, with median age of 25 years.

Table 1. Patients characterstics.

	No (%)
Age, median (range)	25 (14-57)
Transplanted in CR1	62 (56%)
Male	64 (58%)
t (9;11)	6 (5%)
t(v;11)	4 (4%)
Favorable cytogenetic	32 (29%)
Intermediate cytogenetic	55 (50%)
Advers cytogenetic	17 (15%)
Acute GVHD	37 (34%)
Chronic GVHD	49 (45%)

Of the 110 AML patients, 9 (8%) had MLL gene rearrangement. Of these patients, only 5 (4.5% of all patients) had t(9;11). When all patients with MLL rearrangement were considered, patients with MLL abnormality had significantly longer overall survival (OS) (**Figure 1**) when compared with adverse-risk cytogenetics group. However, when patients with t(9;11) were excluded, there was no significant difference in survival (data not shown). In addition, when only patients with the t(9;11) were considered, the t(9;11) patients had significantly longer OS (P=.02) and EFS (P=.03), as compared with patients with adverse cytogenetics including all non-t(9;11) MLL-rearranged cases (Figure 2). MLL rearrangements in the non-t(9;11) group included t(4;11)(q21;q23), t(6;11)(q27;q23) and a variant t(6;11;7)(q27;q23;q11.2), as well as t(11;17)(q23;q25). The survival

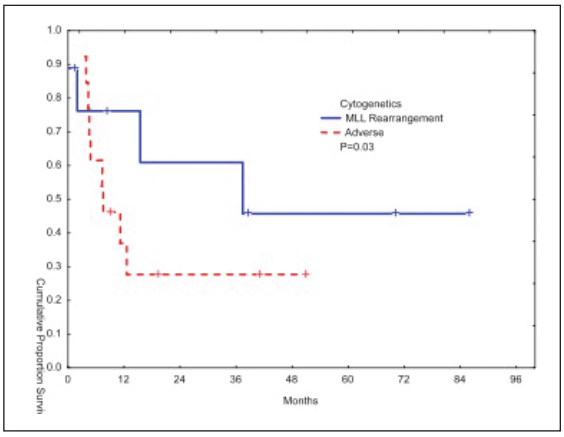

Figure 1. Cumulative proportion surviving, MLL rearrangement patients and patients with adverse cytogenetics.

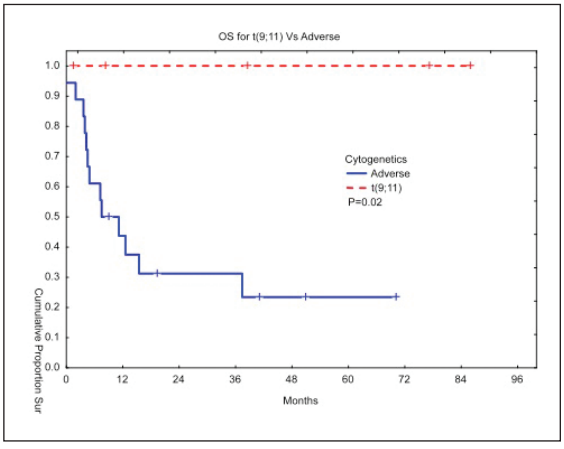

Figure 2. Cumulative proportion surviving, t(9:11) and adverse cytogenetics.

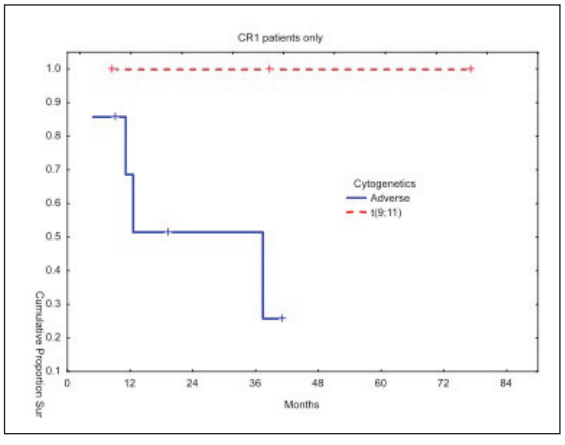

Figure 3. Cumulative proportion surviving, CR1 patients with t(9:11) in and patients with adverse cytogenetics.

for patients with t(9;11) remained significantly longer even when only patients treated with HSCT in first remission were considered (**Figure 3**), although numbers were small. All five patients with t(9;11) were treated with HSCT in CR1.

The data supports the conclusion that MLL-positive t(9;11) AML patients should be classified differently from the rest of the MLL-rearranged cases and should be considered as part of the intermediate-risk group. This classification separating the t(9;11) cases from the rest of the MLL-positive cases should be maintained even when patients are treated with allogeneic HSCT.

Claudia Ulrike Walter,[a] Fahad Al Mohareb,[b] Naeem Chaudhri,[b] Fahad Alsharif,[b] Hazzaa Al Zahrani,[b] Said Mohamed,[b] Walid Rasheed,[b] Abu Jafar Saleh,[b] Wahiba Chebbo,[b] Ghada El Gohary,[b] Mahmoud Aljurf,[b] Maher Albitar[a]

From the [a]Pathology and Laboratory Medicine King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia and [b]Oncology Centre King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Correspondence:
Mahmoud Aljurf, MD
MBC 64 Oncology Centre
King Faisal Specialist Hospital and Research Centre,
PO Box 3354
Riyadh 11211
Riyadh, Saudi Arabia
maljurf@kfshrc.edu.sa

DOI: 10.5144/1658-3876.2012.169

Oral chemotherapy in cancers: what about adherence?

To the Editor: Oral chemotherapy is a convenient treatment option, allowing spacing hospitalizations and avoiding complications of central venous access; however, oral administration raises the problem of adherence, which may compromise effectiveness by not following the proper administration schedule from underdosing or increasing the risk of toxicity from overdosing. We conducted this retrospective case-control study at the National Institute of Oncology in Rabat, from 2008 to 2010, to evaluate factors influencing adherence to oral chemotherapy. All patients treated with capecitabine for breast or digestive cancer for at least six months were included (**Table 1**). Nonadherence was defined as taking less than 90% or more than 110% of the daily dose, missing more than two doses per cycle or not following the administration schedule with an interval between daily doses of less than 8 or more than 12 hours. SPSS version 17 was used for statistical tests with a P value $<.05$ considered significant. Good adherence was observed in 56.3% of patients (**Table 2**). Patients with poor adherence were significantly older, had a lower educational level, and were taking more other chronic medications compared with the rest of our sample. Sex, cancer type and stage had no significant influence on adherence (**Table 3**).

Nonadherence to oral chemotherapy may lead to toxicity, therapeutic resistance and tumor progression. The few studies that have addressed the issue indicate the magnitude of the problem. Poor adherence to tamoxifen was associated with an increased risk of death in breast cancer in one study.[1] In another, adherence to oral cyclophosphamide was only 57% in a breast cancer study.[2] In 108 patients with hematologic malignancies, the adherence rate was 27% for prednisone and only 17% for allopurinol.[3] In a large study involving 2378 patients receiving adjuvant tamoxifen for breast cancer, adherence was 87% during the first year, but only 50% after 4 years.[4]

Good adherence depends on several factors, including the complexity of the medication regimen, side effects, and limited access to drugs.[5] Patients may have a limited understanding of the goals of therapy. Patient education is extremely important to therapeutic results and possible side effects. Poor communication with the medical team is often correlated with poor adherence.[6] In a study involving 384 patients treated for chronic diseases, including cancers, an understanding of the need for treatment was a more powerful factor for greater adherence than clinical signs or socioeconomic level. Apprehension over side effects, as in our study, was correlated with lower adherence rates.[7] Patients with poor compliance to capecitabine were older than the rest of our sample. In a general population, factors associated with nonadherence to oral chemotherapy were low socioeconomic level, institutionalization, and the daily dosage of treatment.[8] Elderly patients may also have cognitive impairment (even minor) and are often underdiagnosed. They often have chronic conditions requiring long courses of treatment that can be confusing in combination with oral chemotherapy. In an ambulatory elderly population, Darnell et al found a compliance rate of 78% for a single long-term medication, 54% for three medications and only 21% for six concomitant medications.[9]

Good adherence to capecitabine